Claims

1. A method for identifying display molecule(s) having affinity towards molecular target(s), comprising the steps of

mixing one or more molecular target(s) associated with target oligonucleotide(s) and a library of bifunctional complexes, each bifunctional complex of the library comprising a display molecule attached to an identifier oligonucleotide, which codes for said display molecule,

coupling to the target oligonucleotide(s) the identifier oligonucleotide of complexes comprising display molecules binding to the target, and

deducing the identity of the binding display molecule(s) and/or the molecular target(s) from the coupled product between the identifier oligonucleotide(s) and the target oligonucleotide(s).

2. The method of claim 1, wherein the display molecule is a reaction product of two or more chemical entities and the identifier oligonucleotide comprises codons identifying the chemical entities.

3. The method of claim 1, wherein one or more members of the library are potentially binding compounds tagged with identifier oligonucleotides.

4. The method according to claim 1, 2 or, 3, wherein the chemical entities are precursors for a structural unit appearing in the display molecule.

5. The method according to any of the claims 1 to 4, wherein some or all of the chemical entities are not naturally occurring α-amino acids or precursors thereof.

6. The method according to claim 1 or 2, wherein each codon comprises 4 or more nucleotides.

7. The method according to claim 1 or 2, wherein the display molecules of the library complexes are non-α-polypetides.

8. The method according to claim 1 to 4, wherein the display molecules of the library complexes are non-nucleic acids.

9. The method according to any of the preceding claims, wherein the display molecule has a molecular weight less than 2000 Dalton, preferably less than 1000 Dalton, and more preferred less than 500 Dalton.

10. The method according to any of the preceding claims, wherein the identifier oligonucleotide uniquely identifies the display molecule.

11. The method according to any of the claims 1 to 10, wherein one or more chemical entities are transferred to the nascent display molecule by a chemical building block further comprising an anti-codon.

12. The method according to claim 11, wherein the information of the anti-codon is transferred in conjunction with the chemical entity to the nascent complex.

13. The method according to any of the preceding claims, wherein the chemical entities are reacted without enzymatic interaction.

14. The method according to any of the claims 1 to 13, wherein the codons are separated by a framing sequence.

15. The method according to any of the claims 1 to 14, wherein the display molecule and the identifier oligonucleotide are joined by a selectively cleavable linker.

16. The method according to claim 15, wherein the linker is cleaved by irradiation.

17. The method according to any of the claims, wherein the library comprises one, two or more different complexes.

18. The method according to any of the claims 1 to 16, wherein the library comprises 1,000 or more different complexes.

19. The method according to claim 1, wherein the molecular target is of a biological origin.

20. The method according to any of the claims 1 to 19, wherein the molecular target is immobilized on a solid support.

21. The method according to claim 20, wherein the target immobilized on the support forms a stable or quasi-stable dispersion.

22. The method according to claim 21, wherein a cleavable linker is present between the solid support and the molecular target.

23. The method according to any of the claims 1 to 22, wherein the molecular target is a protein.

24. The method according to claim 23, wherein the protein is selected from the group consisting of kinases, proteases, phosphatases, and antibodies.

25. The method according to any of the claims 1 to 24, wherein the molecular target is a nucleic acid.

26. The method according to claim 24, wherein the nucleic acid is an DNA or RNA aptamers.

27. The method according to any of the claims 23 to 26, wherein the target protein is attached to the nucleic acid responsible for the formation thereof.

28. The method according to any of the claims 1 to 27, wherein the mixture step includes that a molecular target library comprising different peptides each attached to the nucleic acid responsible for the formation thereof is mixed with a library of complexes.

29. The method according to claim 28, wherein the library of complexes comprises a single bifunctional complex.

30. The method according to any of the claims 1 to 29, wherein the target oligonucleotide is associated by a chemical synthesis to the molecular target.

31. The method according to claim 30, wherein the molecular target is associated with the target oligonucleotide through one or more covalent or non-covalent bonds.

32. The method according to any of the claims 1 to 31, wherein a bifunctional complex having a display molecule binding to the molecular target constitutes the target oligonucleotide associated with the molecular target.

33. The method according to claim 32, wherein the display molecule is a compound known to bind to the target.

34. The method according to claim 33, wherein a target is saturated with a known ligand prior to the mixing step.

35. The method according to claim 34, wherein the target oligonucleotide is associated with the molecular target during the mixing step.

36. The method according to claim 35, wherein two bifunctional complexes of a library of bifunctional complexes are associated with a common molecular target.

37. The method of claim 36, wherein the bifunctional complexes bind to the same binding site of the molecular target.

38. The method of any of the claims 31 to 36, wherein the bifunctional complexes bind to discrete binding sites.

39. The method according to any of the preceding claims, wherein an initial ligand or a pool of ligands with potential affinity towards a target is amended by reaction with one or more chemical entities to form a second generation library, said second generation library being used in the method according to any of the claims 1 to 39.

40. The method according to any of the preceding claims, wherein two or more targets interacting in a biological context separately are subjected to the method of claim 1, whereupon the identified display molecules binding to the two or more targets are linked via a suitable linker.,

41. The method according to any of the claims 1 to 40, wherein two or more molecular targets or type of molecular targets are involved in the mixing step and the target oligonucleotide identifies the molecular targets or the type of molecular targets.

42. The method according to any of the claims 1 to 41, wherein the mixing step includes the removal of non-binding library members prior to the coupling of the target oligonucleotide and the identifier oligonucleotide together.

43. The method according to any of the previous claims, wherein the target oligonucleotide and/or the identifier oligonucleotide partly or fully is hybridised to a complementing oligonucleotide.

44. The method according to any of the claims 1 to 43, wherein the coupling is performed using means selected from the group consisting of chemical means, enzymatic means, and design means.

45. The method according to any of the claims 1 to 44, wherein the target oligonucleotide or a complementing target oligonucleotide and the identi-

fier oligonucleotide or a complementing identifier oligonucleotide operatively are joined together so as to allow for a polymerase to recognise the coupled strand as a template.

46. The method according to any of the preceding claims, wherein the enzymatic means are selected from enzymes of the type polymerase, ligase and restriction enzyme, and any combination thereof.

47. The method according to claim 46, wherein a ligase is used to join the target oligonucleotide and the identifier oligonucleotide together.

48. The method of claim 47, wherein a connector oligonucleotide having a region complementing a distal part of the target oligonucleotide and a region complementing a distal part of the identifier oligonucleotide is used during the coupling step so as to allow a ligase or a combination of a ligase and a polymerase to join the identifier and target oligonucleotides together.

49. The method according to claim 48, wherein the ends of the oligonucleotides abut each other.

50. The method according to claim 49, wherein the region of the connector oligonucleotide complementing a distal part of the identifier and/or target oligonucleotide is 6 to 16 nucleotides.

51. The method according to claims 49, wherein the region is 8 to 12 nucleotides.

52. The method according to claim 48, wherein the connector oligonucleotide is added in excess.

53. The method according to any of the claims 1 to 46, wherein a region at the distal ends of the target and identifier oligonucleotides are complementary to each other and a polymerase is allowed to extend the target and/or the identifier oligonucleotide.

54. The method according to any of the claims 1 to 47, wherein the target oligonucleotide and/or the identifier oligonucleotide is provided with a sticky end to allow a ligase or a polymerase or a mixture thereof to adjoin the oligonucleotides.

55. The method according to claim 54, wherein the sticky end is formed by a restriction nuclease.

56. The method according to any of the claims 1 to 55, wherein the target and the identifier oligonucleotide or sequences complementary thereto at the proximal end is provided with a priming site.

57. The method according to any of the claims 1 to 56, wherein the target-display conjugate is recovered by chromatography following the coupling of the target and the identifier oligonucleotides.

58. The method according to claim 57, wherein the chromatography is size-exclusion chromatography.

59. The method according to claim 1, wherein the coupled identifier and target oligonucleotide is amplified prior to decoding the identity of the display molecule.

60. The method according to any of the claim 1, wherein the coupled oligonucleotide is amplified by PCR using priming sites positioned proximal to the display molecule and the molecular target, respectively.

61. The method according to claim 59, wherein selective cleavable chemical moieties in each end of the coupled oligonucleotides are cleaved to liberate the coupled oligonucleotide prior to amplification.

62. The method according to any of the claims 1 to 61, wherein the coupled oligonucleotide is recovered and subjected to amplification.

63. A conjugate comprising a molecular target associated with an oligonucleotide and a bifunctional complex comprising a display molecule attached to an identifier oligonucleotide, which codes for said display molecule.

64. The conjugate of claim 63, wherein the display molecule is bound to the target.

65. The conjugate according to claims 63 or 64, wherein the target oligonucleotide and/or the identifier oligonucleotide are joined to the molecular target and/or the display molecule, respectively, through a selectively cleavable link.

66. The conjugate according to any of the claims 63 to 65, wherein the target oligonucleotide is coupled to the identifier oligonucleotide.

67. The conjugate according to claims 66, wherein the coupled oligonucleotide is amplifiable.

68. A display molecule identified by the method according to any of the claims 1 to 62.